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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,867	02/08/2002	Sang-Gu Lee	5294-000004	8718

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EXAMINER

MOSHER, MARY

ART UNIT PAPER NUMBER

1648

DATE MAILED: 06/10/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/071,867

Applicant(s)

Lee et al

Examiner

Mosher

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 4/24/2003, 5/10/2002,
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above, claim(s) 21 and 52-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 and 22-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some\* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6 6) ☐ Other:

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## **DETAILED ACTION**

### ***Election/Restriction***

Applicant's election with traverse of group I in Paper No. 8 is acknowledged. The traversal is on the ground(s) that "both groups of claims are drawn to subject matter which are so related to each other than an undue burden would not be placed upon the Examiner by maintaining both groups of claims in a single application." This is not found persuasive because the search required for each of the groups is different. Group I involves an active step of mutating an insert to alter certain characteristics, whereas group II requires inserting a nucleic acid which naturally possesses certain characteristics. The group II invention requires burdensome search of all existing constructs where a sequence is inserted in a single-stranded RNA virus vector (if any contain naturally-occurring sequences with the characteristics recited in the claim, then the construction of those would anticipate group II but not group I claims). This search is not required for group I. Group III has no search in common with group I, being drawn to a totally different method.

The requirement is still deemed proper and is therefore made FINAL.

Claims 21 and 52-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups, there being no allowable generic or linking claim. Claims 20, 23-25, and 30-51 have been examined only to the extent that they read upon the elected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

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### *Claim Objections*

Claims 11, 18, 38 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 is identical to parent claim 10. Claim 18 is identical in scope to parent claim 15, because "monomeric, dimeric, or multimeric" cover all the possibilities for an insert. If there is not any embodiment of claim 15 that is outside the scope of claim 18, then claims 15 and 18 are identical in scope, even if differently worded. Claim 38 has the same problem.

Claim 19 is objected to because of the following informalities: the typo "hetero-dimmer". Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

Claims 1, 2, 4-11, 15-20, 22, 23, 25-31, 35-42, 46-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for improving genetic stability of a recombinant poliovirus vector, does not reasonably provide enablement for a method for improving genetic stability of any single-stranded RNA virus vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

These claims are broadly drawn to a "single-stranded RNA virus vector." There are many different single-stranded RNA viruses, and they form a very diverse group, see for example

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Strauss et al, pages 162-169 ( Fields Virology, third edition, ed. B.N. Fields, pages 153-171, Raven publishers, Philadelphia, 1996). Rima et al (Journal of General Virology 78:2859-2870, 1997) teaches that G+C content varies from about 30% to about 70% in single-stranded RNA viruses, see Figure 3 for example. Jenkins et al (Journal of Molecular Evolution 52:383-390, 2001) also teaches that G+C content is strikingly different among different RNA viruses, and in the Flavivirus genus, the G+C content is correlated with different animal hosts. Jenkins points out that "Since all three families of RNA viruses [in this study] replicate in the cytosol using their own polymerase, distinct mutational biases could be explained by differences in their viral polymerase or in the cytosolic ribonucleotide pools of their target cells." Strauss et al states, in a discussion of G+C content in DNA viruses, "Even if the altered G+C content of many viruses arises from biases introduced by their own polymerases during replication, however, it must in addition confer a selective advantage, or it would not have been maintained throughout evolution." This logic applies with equal force to RNA viruses. Therefore, those skilled in the art believe that different selective forces act upon different RNA viruses, resulting in different G+C content in the viral genomes. One skilled in the art would not unquestioningly accept an assertion that a change in G+C content would have the same biological effect in all single-stranded RNA viruses, since the different viruses respond to different selective forces. Since the specification only provides evidence of unexpected stabilization of inserts in polioviruses, it is concluded that the enabling disclosure is commensurate only with polioviruses. Considering the broad scope of the claims, the widely varying nature of single-stranded RNA viruses, the unpredictable biological

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effects of GC content changes in different families of viruses, and the limited scope of the working examples, it is concluded that undue experimentation would be required to enable the full scope of the invention as claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-20, 22-51 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Lee et al (Journal of Virology 76(4):1649-1662, issue received on January 25, 2002). Lee is available as prior art, because the authorship of the paper is not identical to the inventorship of this application, because it was published before this application was filed, and because applicant has not provided a certified translation of the Korean priority document.

Claims 1, 4, 9, 15, 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Parrington US 6060308. Parrington teaches a single-stranded RNA viral vector (the alphavirus SFV) with an RSV F gene insert. Parrington performs a mutagenesis on the F gene sequence which increases the G/C content by one nucleotide without causing amino acid substitution, see Examples 1 and 2. The G/C content was about 36% after the mutagenesis. Since Parrington performed the same active step as recited in the claim, Parrington anticipates the invention as claimed, even if Parrington performed the same step for a somewhat different purpose. Claim 20

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and dependent claims are not included in this rejection because the SFV vector, while capable of replicating the genomic RNA, lacks the coat protein genes needed for viral propagation.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-7, 9, 15, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parrington US 6060308 in view of Mason et al WO 02042326. Mason is available as prior art with an effective date of 22 November 2000. Parrington teaches an alphavirus vector containing an inserted RSV F gene. This differs from the claimed invention in that Parrington did make major alterations in the G/C content of the insert. However, Mason teaches that the RSV F gene has suboptimal codons for expression in mammalian cells, that the natural F gene sequence is

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approximately 65% AT while most mammalian expressed genes are <50% AT. Mason teaches optimized expression of the RSV F gene by replacing A/T rich regions with G/C rich sequences. See for example pages 87, 30-31, and 33. It would have been within the ordinary skill of the art to use the optimized RSV F sequence of Mason in the alphavirus vector of Parrington, for the purpose of improving expression of the desired F protein, with reasonable expectation of success. Furthermore, while Parrington teaches SFV as the preferred alphavirus, the reference broadly teaches any alphavirus, and Venezuelan Equine Encephalitis virus is a well-known alphavirus vector. Therefore the invention as a whole is prima facie obvious, absent unexpected results. It is noted that applicant showed unexpected stabilization of a poliovirus vector; however, this showing is not commensurate in scope with the claimed subject matter.

*Allowable Subject Matter*

If the rejection over Lee et al is obviated, claims 3 and 12-14 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and claims 24, 32-34, 43-45 and 51 would be allowable if limited to the elected invention and rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: Aside from Lee et al, the prior art does not teach or suggest that modification of the G/C content or G/C distribution in the foreign insert of a poliovirus vector would improve the ability of the vector to stably retain the insert through multiple rounds of viral propagation.



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*Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone numbers for this Group are now (703) 872-9306 for Before Final responses, and (703) 872-9307 for After Final responses. Faxes for this Group can also be sent to (708) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 9, 2003


  
**MARY E. MOSHER**  
**PRIMARY EXAMINER**  
**GROUP 1800-1600**

**APPENDIX: Finding WIPO publications and determining IA filing date, US designation and publication language (continued)**

Ex. 2 (cont.): Because the US application publication is based on an international application (PCT) filed on or after 11/29/00, published in English and the IA designated the US, the examiner may apply the reference under § 102(e) as of:

14 January 2000\*

\* assumes proper support for the claimed subject matter in the 111(b) provisional application.

		(10) International Publication Number	WO 01/52541 A1
		(43) International Publication Date	19 July 2001 (19.07.2001)
PCT			
(21) International Application Number	PCT/IL01/00035		
(22) International Filing Date	14 January 2001 (14.01.2001)		
(25) Filing Language	English		
(26) Publication Language	English		
(30) Priority Data:			
60/176,215	14 January 2000 (14.01.2000)	US	
60/179,968	3 February 2000 (03.02.2000)	US	

**APPENDIX: Applying § 102(e) Prior Art Date for Publications & Patents Five Guidelines (Positive 1, 2 & 3 and Negative 4 & 5)**

1. If U.S. patent or U.S. application publication issued from an application under 35 USC § 111(a), and the patent or application does not claim a benefit of an IA, the patent or application publication has a § 102(e) prior art date as of the earliest U.S. effective filing date. See Examples A1A, A1B, P1.
2. If the U.S. patent, U.S. application publication, or WIPO publication issued from, or claims benefit to, an IA which has an international filing date on or after 11/29/00, designated the United States, and was published in English by WIPO (under PCT Article 21(2)) the § 102(e) date is the international filing date, or any earlier effective U.S. filing date.

See examples A2A-A2C and P2A-P2C.

3. Guideline 3. If the U.S. patent issued from, or claims benefit to, an IA which was filed on or after 11/29/00, but the WIPO publication was not in English, the U.S. patent: if issued from the 35 USC § 371 application, has no § 102(e) date, or if issued from a U.S. continuing application claiming benefit of the IA, has the § 102(e) date of the filing date of a later-filed continuing U.S. application. See Examples P3A-P3C.